UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,119	04/13/2007	Timothy Charles Ramsey Prickett	36697.17	1813

27683 7590 02/20/2009

HAYNES AND BOONE, LLP
IP Section
2323 Victory Avenue
Suite 700
Dallas, TX 75219

EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
02/20/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,119	PRICKETT ET AL.	
	Examiner	Art Unit	
	JAMES L. GRUN	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21,23-33,35,36 and 44-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21,23-33,35,36 and 44-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/24/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The amendment filed 24 November 2008 and the declaration of Timothy Charles Ramsey Prickett under 37 CFR 1.132, filed 24 November 2008, are acknowledged and have been entered. Claims 44-51 are newly added. Claims 22, 34, and 37-43 have been cancelled. Claims 1-21, 23-33, 35, 36, and 44-51 remain in the case.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1-21, 23-33, 35, and 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With regard to these claims, the specification, as originally filed, does not provide support for "other than an adult in congestive heart failure" as is now claimed for the subject. Although one of skill in the art might realize from reading the disclosure that adults with heart failure have elevated levels of the N-terminal fragment of pro-C-type natriuretic peptide (NT-proCNP) in plasma (see e.g. Fig. 4), such determinations do not provide explicit or implicit indication to one of skill in the art that possible exclusion of this group of patients was originally

contemplated as part of applicant's invention and such possibility does not satisfy the written description requirements of 35 U.S.C. § 112, first paragraph. Note that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement. Indeed, the only subject populations suggested for exclusion in the application as filed appear to be those with renal diseases or disorders (see e.g. Specification, pages 14-15), , not heart failure subjects as are now claimed. Applicant is requested to direct the Examiner's attention to specific passages where support for these newly recited limitations can be found in the specification as filed or is required to delete the new matter.

Claims 1-21, 23-28, and 44-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, particularly the invention commensurate in scope with these claims.

Applicant's specification, while describing and being enabling for determination of skeletal development in pre-adults, and in those suspected of having a skeletal disease or disorder, with determinations of the N-terminal fragment of pro-C-type natriuretic peptide (NT-proCNP) levels in plasma compared to levels in one or more control populations matched, for example, in age and sex, does not reasonably provide description or enablement for determinations indicative of skeletal disease or disorder in subjects with differences from a

control population level generally. Absent further guidance from applicant, one would not be assured of the ability to practice the invention without comparison to a relevant control. For example, one would not be able to determine abnormal growth by comparing the level in a pre-adult to levels in adults (i.e. a control having a known first skeletal growth information of having attained maximum skeletal growth).

The specification is objected to and claims 1-7, 14-20, 28-32, 36, 44, and 48 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons of record that the specification, while being enabling for anti-NT-proCNP antibodies for use in immunoassays, does not reasonably provide written description or enablement for a method of measuring the N-terminal fragment of pro-C-type natriuretic peptide (NT-proCNP) or binding agents therefor generally. As set forth, applicant teaches only immunoassay detection of the fragment. As also set forth, absent further written description and guidance from applicant, one would not know or be able to predict what other method functions to specifically detect the peptide fragment other than an immunoassay with the specific antibodies. Moreover, for the reasons of record, the specification does not provide sufficient recitation of distinguishing identifying characteristics of the genus of binding agents other than for antibody populations specific for NT-proCNP which predictably function to detect NT-proCNP peptides. Thus, the specification does not provide sufficient written description to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Applicant's amendments, the declaration under 37 CFR 1.132 filed 24 November 2008, and/or applicant's arguments thereto have been fully considered and are sufficient to overcome

the rejection of the claims under 35 U.S.C. § 112, first paragraph, based upon prior questions regarding the sufficiency of the disclosure to describe and enable the scope of the invention as claimed with regard to biological samples and antibodies.

Applicant's arguments filed 24 November 2008 have been fully considered but they are not deemed to be persuasive with regard to the issues set forth in the restatement of the rejection above. Notwithstanding applicant's assertions to the contrary, applicant's amendments have not obviated rejections under this statute for the reasons set forth above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15 and 29-32 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 15, the interrelationships of the components for comparison are not clear, e.g. it is not clear if a single mean derived from a population of multiple ages or multiple means derived from populations of known similar ages are used in the comparing step.

In claim 29 and claims dependent thereupon, recitations of "the" level or rate lack antecedent basis.

Applicant's arguments filed 24 November 2008 have been fully considered but they are not deemed to be persuasive.

Notwithstanding applicant's assertions to the contrary, applicant's amendments have not obviated rejections under this statute for the reasons set forth above.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6-9, 11-17, 21, 24-28, 33, and 36 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Prickett et al. (Biochem. Biophys. Res. Comm. 286: 513, 2001) for reasons similar to those of record. In addition to the teachings of the reference set forth in the prior Office action, the examiner would note that the adult control population of the reference inherently had obtained maximum skeletal growth. Moreover, in this population, individual measurements were compared to the mean (e.g. to calculate a standard error of the mean).

Applicant's arguments filed 24 November 2008 have been fully considered but they are not deemed to be persuasive.

Notwithstanding applicant's assertions to the contrary, for the reasons of record the reference performed all of the positively recited process steps as instantly claimed, i.e. levels of the N-terminal fragment of pro-C-type natriuretic peptide (NT-proCNP) were measured in adult human plasma samples and the individual measurements were compared to the mean (e.g. to calculate a standard error of the mean). Notwithstanding applicant's assertions to the contrary, a clause merely reciting a desired result of a positively recited process step is not given weight. For example, measurements in additional normal samples would not be changed significantly from the previously determined normal mean or range. With regard to the kit (claims 33 and 35) and the binding agent (claim 36) claims, the examiner would note that: a recitation of intended use is accorded patentable weight only to the extent that it limits the actual components of a

composition; and, in the instant case the intended use does not affect the components in any way which distinguishes over the subject matter taught or suggested by the reference. Moreover, the printed matter in no way depends on the kit, and the kit components in no way depend on the printed matter. All the printed matter does is to teach an alternative use for an existing product. As pointed out in In re Gulack 703 F2d 1381 (Fed Cir. 1983), "[w]here the printed matter is not functionally related to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability."

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1, 2, 6-17, 21, 23-28, 33, 35, and 36 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Prickett et al. (Biochem. Biophys. Res. Comm. 286: 513, 2001) in view of Buechler (US 2003/0219734) for reasons, set forth below, that are similar to those of record in the prior rejection of these claims.

The teachings of Prickett et al. and Buechler are as set forth previously and/or above. The teachings of Prickett et al. differ from the invention as instantly claimed in not teaching monoclonal antibodies specific for NT-proCNP.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have substituted monoclonal antibodies and alternative assay formats such as sandwich immunoassays, as taught in Buechler, for the polyclonal antibodies and competitive assay in Prickett et al. because to do so is notoriously old and well known in the art. It would have been obvious to have generated monoclonal antibodies in order to provide a potentially unlimited source of homogeneous reagent specific for defined epitopes of the peptide in order to detect particular fragments of C-type natriuretic peptide as taught in Buechler.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Applicant's arguments filed 24 November 2008 have been fully considered but they are not deemed to be persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this regard, applicant urges that Buechler does not specifically teach antibodies specific for the peptides taught in Prickett et al. for use. This is not found persuasive because the relevant peptides, as admitted by applicant, are taught in Prickett et al. and because the reference of Buechler clearly teaches the use of

antibodies to fragments such as peptide fragments of pro-C-type natriuretic peptide comprising at least 6 contiguous amino acids of CNP_{1-73} (see pages 3-7, particularly page 4).

Applicant's amendments, the declaration under 37 CFR 1.132, and/or applicant's arguments thereto, filed 24 November 2008, as related to the predictability of success for assessing skeletal growth with biological fluid levels of NT-proCNP are sufficient to overcome the prior rejection of claims under 35 U.S.C. § 103(a) based upon the combination of Prickett et al. (Biochem. Biophys. Res. Comm. 286: 513, 2001) in view of Buechler (US 2003/0219734), Yasoda et al. (J. Bone Min. Res. 15(Suppl. 1): S243, 2000), and Chusho et al. (Proc. Natl. Acad. Sci. USA 98: 4016, 2001).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 11 a.m. to 7 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, SPE, can be contacted at (571) 272-0806.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/J. L. G./
James L. Grun, Ph.D.
Examiner, Art Unit 1641
February 20, 2009

/Ann Y. Lam/
Primary Examiner, Art Unit 1641
February 13, 2009